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OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

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MEMORANDUM

Date: **December 22, 2010**

SUBJECT: **Dicamba.** Waiver Request for Proposed New Salts

PC Code: 029801
Decision No.: 436860
Petition No.: NA
Risk Assessment Type: NA
TXR No.: NA
MRID No.: 481442-01 to -03

DP Barcode: D381326
Registration No.: NA
Regulatory Action: New Registration
Case No.: NA
CAS No.: 1918-00-9
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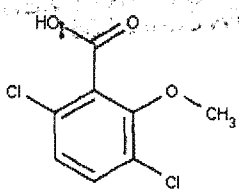
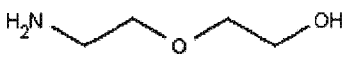
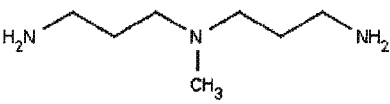
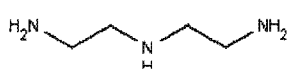
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BASF has submitted a pre-application study plan and waiver request for two proposed salts of the herbicide dicamba. There are several salts of dicamba currently registered, but BASF would like to register two additional formulations that will contain the BAPMA (N,N-bis-(3-aminopropyl)methylamine) and DETA (N-(2-aminoethyl)-1,2-ethanediamine) salts of dicamba. BASF is pursuing registration for these two salts because in laboratory and field trials they have demonstrated lower volatility and less non-target impact than the currently registered dicamba salts. Structures of dicamba, its diglycolamine (DGA) salt and the proposed new salts may be found in Table 1. The registrant has submitted a proposal for conducting residue chemistry and

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toxicology studies (MRID 48144201) to support these registrations and the Registration Division has requested HED comment on their proposal.

Table 1. Structures of Dicamba and Proposed New Salts		
Common Name	Structure	CAS Chemical Name
Dicamba		3,6-dichloro-2-methoxybenzoic acid or 2-methoxy-3,6-dichlorobenzoic acid
Diglycolamine		2-(2-Hydroxyethoxy)ethylamine
BAPMA		N,N-bis-(3aminopropyl)methylamine
DETA		N-(2-aminoethyl)-1,2-ethanediamine

CONCLUSIONS

The study plan that the registrant has proposed for the residue chemistry studies is appropriate and requires no further modification. In addition to the acute toxicity and mutagenicity studies suggested by the registrant HED recommends the registrant also conduct a subchronic feeding study and developmental testing in one species. Due to the corrosive nature of the cations, a subchronic dermal and inhalation study should also be conducted.

DETAILED CONSIDERATIONS

Toxicology

BASF Proposal

Dicamba salts rapidly dissociate to dicamba and the corresponding cation (MRIDs 43288001 and 48144202). The registrant has reported summaries of preliminary toxicity testing for the BAPMA and DETA cations, as described below.

BAPMA is reportedly in toxicity category III for acute oral exposure, is in tox category I for acute dermal exposure, is in tox category II for acute inhalation exposure, and is corrosive to skin and eye. DETA is reportedly in tox category III for oral exposure, is in tox category II for dermal exposure, is corrosive to skin and eye, and is a dermal sensitizer. The kidney is

reportedly a potential target organ for DETA based on results from the acute oral toxicity study, although no more details were given. The OECD 421/422 reproduction/developmental toxicity screening test was reportedly negative for fertility effects. Preliminary mutagenicity testing for BAPMA and DETA did not result in any mutagenicity concerns.

The registrant has proposed testing the BAPMA and DETA salts of dicamba with a battery of acute toxicity tests and mutagenicity tests. Depending upon results of the acute studies, the registrant has proposed tier I contingency testing of an abbreviated side-by-side ADME study with the dicamba salts. Tier II contingency testing would consist of a 90-day toxicity study in rats with the dicamba salt.

HED Comment

Testing of the BAPMA and DETA salts should include the acute toxicity and mutagenicity studies suggested by the registrant. Acute studies do not always provide an indication of toxicity which may occur after longer term treatment (although there was reportedly an indication that the kidney was a target after acute treatment with DETA). For this reason, a minimum database for bridging typically also requires a developmental toxicity study and a subchronic toxicity study.

There are also concerns about portal of entry toxicity which could occur due to the corrosive nature of the cations. Therefore, the registrant should also conduct a subchronic dermal and inhalation study for each salt, in addition to the subchronic study and developmental study.

Residue Chemistry

BASF Proposal

The metabolism in plants and animals is adequately understood for dicamba on the basis of studies with the currently registered salts on soybean, asparagus, cotton, sugarcane, and published data on grass. In the majority of registered crops, the major metabolite is 3,6-dichloro-5-hydroxy-o-anisic acid. Established tolerances are expressed as the dicamba parent plus this major metabolite. Therefore, BASF does not plan to conduct any additional metabolism studies for the new salts of dicamba.

As part of the residue chemistry data requirements for the currently registered dicamba salts, BASF has provided analytical methods that have been independently validated for detecting and measuring levels of dicamba and its metabolites in or on food. The limit of detection allows monitoring of food with residues at or above the levels described in the existing tolerances. No additional analytical methods are required for analysis of the new dicamba salts.

Crop field trials have been previously conducted with dicamba on various crops with different amine salts of dicamba. The studies were conducted in geographical representative areas. Results from testing multiple dicamba salts in side-by-side trials confirm that no effect on magnitude of the residues was caused by the salt formulation type of dicamba. Tolerances have already been established under for livestock commodities. The registrant believes there is no

reason to expect that different salts will result in quantifiable residues above the limits of the established tolerances.

In order to verify that the new salts do not differ in residue from the registered dicamba salts, BASF will conduct limited number of bridging studies. BASF will test BAPMA, DETA, and DGA salts side by side in a small number of trials in corn, wheat, and pasture grass.

HED Comment

HED concurs with the registrant that new metabolism and analytical method studies are not needed to support the registration of the new salts. HED also agrees that the commodities the registrant intends to test in the limited crop field trials are appropriate. If residues are significantly higher on the crops treated with the new salts, then a full set of residue data may be needed. HED will assess the need for modifying the livestock commodity tolerances once the new residue data are received.